Protocol Title: Real World Administration of Zepatier (Grazoprevir plus Elbasvir) in Chronic Hemodialysis Patients with Hepatitis C Infection. Strategies for Identification of Candidate Hemodialysis Patients, Obtainment of Insurance Approval, Treatment Guidelines, and Laboratory and Clinical Monitoring During Therapy Directed to Nephrologists

NCT Number: 03365635

IRB Approval Date: August 13, 2018

Document: Protocol August 18, 2021

Investigator Studies Program (MISP) Protocol Template

Requirements for Submitting a Full Proposal

Section #1 - MISP Protocol Identification

Study Title:	**"Real World" Administration of Zepatier (Grazoprevir plus Elbasvir) in Chronic Hemodialysis Patients with Hepatitis C Infection. Strategies for Identification of Candidate Hemodialysis Patients, Obtainment of Insurance Approval, Treatment Guidelines, and Laboratory and Clinical Monitoring During Therapy Directed to Nephrologists**
Request Date:	**September 9, 2016 Modified July 14, 2018**
Institution Name	Penn Presbyterian Medical Center
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Section #2- Core Protocol	
2.1 Objectives & Hypotheses	Objective - The primary objective is to develop "real world" strategies for the successful treatment of hepatitis C hemodialysis patients using Zepatier in a hemodialysis unit with a high prevalence of hepatitis C to improve patient outcomes and to reduce the risk of in-facility transmission of hepatitis C. These strategies developed will be primarily directed to Nephrologists and Hemodialysis Personnel (Nurses, Social Workers, Dieticians) in order that these individuals will gain the knowledge to administer a hepatitis C eradication program using Zepatier in their hemodialysis centers Hypothesis – Hemodialysis patients have an increased prevalence of hepatitis C infection. Zepatier has been shown to be highly efficacious in the treatment of hepatitis C in hemodialysis patients. Current guidelines targeted to nephrologists for treatment of hepatitis C hemodialysis patients which incorporate DAAs have not been published. The hypothesis of this protocol is that guidelines for successful treatment of hemodialysis patients using current therapies such as Zepatier which can be implemented and managed primarily by nephrologists and hemodialysis personnel.
2.2 Background & Rationale, Significance of Selected Topic & Preliminary Data	1. Hemodialysis patients have an exceptionally high prevalence of hepatitis C, with prevalence rates up to 25% in urban hemodialysis units in the United States and greater than 50% in less developed countries. 2. It has been estimated that by 2020, 775,000 patients with ESRD will need dialysis in the United States and 109,000 of these patients will be infected with hepatitis C. 3. Hepatitis C is associated with an increased mortality among hemodialysis patients with a relative risk of 1.59 (95% CI, 1.33- 1.86). 4. Kidney transplant recipients with hepatitis C also have an increased mortality with a relative risk of 1.79 (95% CI. 1.57-2.03). In addition hepatitis C infected transplant patients have an increased death rate from infection in the early (< 6 months) post-transplant period and a decreased graft survival. 5. Attempts to prevent nosocomial transmission of hepatitis C in dialysis units by implementing universal precautions have not been consistently successful. 6. The introduction of direct acting antivirals (DAAs) in 2011 as a treatment of hepatitis C patients has created a paradigm treatment shift for these patients. The DAAs have been shown to be highly effective with SVR rates greater than 90 to 95% in

treatment naïve hepatitis C infected patients in the general population

7. One DAA, Zepatier is well suited for treatment of hemodialysis patients as well as patients with stage 4 or 5 chronic kidney disease not requiring hemodialysis since less than 1% of this DAA is excreted by the kidney. A recent randomized double-blind multicenter study compared Zepatier to placebo in stage 4 and 5 chronic kidney disease patients most of whom were hemodialysis dependent (77%) and who had infection with hepatitis C genotype 1. A SVR at 12 weeks after the end of therapy was achieved in 99% of patients who received Zepatier.

8. The majority of hemodialysis patient care is provided by nephrologists and hemodialysis healthcare personnel. Both of these caregiver groups have become quite adept at providing protocol driven medical care uniquely suited to this population and care setting. Although hemodialysis patients often have primary care providers and other medical specialists who participate in their care, dialysis patients are often reluctant to see these non-Nephrology physicians due to their demanding dialysis schedule. Furthermore, non-Nephrology providers often feel uncomfortable providing care and prescribing medications to patients with severely impaired renal function.

9. Thus, nephrologists and hemodialysis personnel are uniquely situated to implement and monitor treatment protocols using DAAs such as Zepatier in dialysis unit patients with hepatitis C infection. Clear and current guidelines for the implementation and monitoring of DAA treatment protocols in the hemodialysis population currently do not exist, and the development of such guidelines is one of the purposes of this protocol.

10. While nephrologists and hemodialysis health care personnel are aware of the prevalence of hepatitis C in hemodialysis patients and that DAAs are now available for treatment of such patients, most nephrologists and hemodialysis personnel are not aware of the specific "real world" steps required to identify and treat such patients

11. Another purpose of this protocol is to provide the specific "real world" steps which must be taken to successfully treat hepatitis C hemodialysis patients with DAAs. Application of these steps will allow hemodialysis units to implement guidelines which will allow DAA treatment of all eligible patients in a timely manner, thus reducing or eliminating the health consequences of hepatitis C infection is this special population.

12. This "real world" protocol will be developed and implemented by a diverse group of investigators, each with a unique area of expertise needed for such a protocol development with "real world" implementation. Members of the investigative

	team include physicians with expertise in nephrology, hepatology, infectious disease, infection control, transplant nephrology and non-physician personnel with expertise in clinical pharmacology and hemodialysis social services. 13. The specific "real world" measures to be developed and summarized in this protocol are: a. Identify hepatitis C patients who meet the virologic and medical criteria for treatment with Zepatier alone or in combination with ribavirin b. Identify necessary pretreatment clinical and laboratory assessments that are needed before initiating treatment with Zepatier including those necessary for third party payment approval. c. Identify appropriate treatment candidates and obtain third-party payment approval. d. Identify clinical and laboratory testing to monitor during treatment. e. Perform post-treatment testing of sustained virologic response to treatment (SVR at 12 weeks). f. Identify barriers to third-party payment of treatment and steps necessary to overcome these barriers. g. Identify the roles of a clinical pharmacologist and non-physician health care personnel such as a dialysis nurse, social worker, and dietician in a Zepatier treatment protocol of hepatitis C infected dialysis patients. h. Identify available patient assistance programs for drug obtainment and criteria needed to qualify for such assistance.
2.3 Study Design	This is an interventional, prospective, non-randomized, non-blinded trial to evaluate real world strategies to identify and treat hepatitis C infected hemodialysis patients with Zepatier. Based on a recent surveillance evaluation, there are approximately 30 patients in the hemodialysis unit with hepatitis C antibody of whom approximately 25 will qualify for therapy with Zepatier alone or in combination with Ribavirin. Patients with known HCV infection defined by positive anti-HCV ab (prevalent positives) will be identified from review of the dialysis unit electronic medical records. All anti-HCV antibody positive patients will undergo HCV quantitative RNA testing. Those found to have detectable HCV RNA will undergo HCV genotyping. Patients who are hepatitis C PCR positive will proceed into additional screening and will sign a consent form at this time.

Other Inclusion Criteria

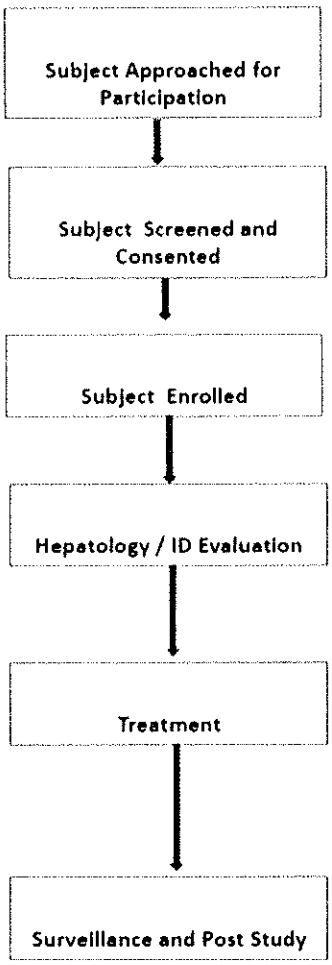
a. Age: Be greater than 18 on day of signing informed consent
b. HCV treatment status must fall into one of following categories (1) Naïve to all anti HCV treatment (2) Prior INF or PEG IFN + ribavirin treatment failures (null responders, partial responders, relapses) (3) Intolerant to prior INF or PEG-INF + ribavirin regimen (4) Prior HCV NS3/4A protease inhibitor failures.
c. Not of reproductive potential – hemodialysis patient with 12 months of no menses. Women of childbearing potential should use 2 reliable forms of contraception simultaneously during treatment and for 6 months after completion of therapy. This guideline will be applied for both Zepatier treatment alone or when combined with Ribavirin.
d. Males with partners of reproductive potential as long as contraception is used during and for 6 months after completion of therapy. This guideline will be applied for both Zepatier treatment alone or when combined with Ribavirin.
e. Understand the study procedures, alternative treatments available, risks involved with the study, and voluntarily agrees to participate by giving informed written consent.

Exclusion Criteria

a. Unable to provide informed consent
b. Currently undergoing active treatment with a direct acting antiviral agent
c. Have previously undergone successful treatment with a direct acting antiviral agent
d. Have moderate or severe hepatic impairment (Child-Pugh B or C)
e. Have evidence of decompensated liver disease manifested by presence or history of ascites, gastric or variceal bleeding, hepatic encephalopathy, or other signs/symptoms of advanced liver disease
f. Co-administration of known Hepatotoxic Drugs including but not limited to
(1) Etofoxine
(2) Isoniazid
(3) Nitrofurantoin
(4) Phenytoin
g. Patients receiving strong CYP3A/P-gp inhibitors, organic acid transporting polypeptide 1B1/3 inhibitors, strong inducers of cytochrome 450 3A (CYP3A), efavirenz, and other drugs which may interact as per Zepatier package insert.
h. Has a history of substance abuse with alcohol, intravenous

	drugs, psychotropics, narcotics, cocaine use within 1 year of screening or if shorter, is judged by the investigator to be capable of complying with study procedures. i. Has a history of any condition, pre-study laboratory abnormality, or ECG abnormality or history of any illness which in the opinion of the investigator might confound the results of the study or pose additional risks from the administration of study drugs. j. Has evidence or history of chronic hepatitis not caused by HCV including but not limited to nonalcoholic steatohepatitis (NASH), drug induced hepatitis, and autoimmune hepatitis. k. Patients currently on a kidney transplant waiting list who have agreed to accept HCV positive organ offers. l. All patients currently undergoing kidney transplant evaluation. m. Laboratory Exclusion values# (1). Hemoglobin less than 9 g/dL if patient will require concomitant ribavirin therapy (2). Neutrophils less than 1,500/uL in Caucasians or less than 1,200/uL in Blacks (3). Platelets less than 70,000/uL (4). Direct bilirubin greater than 1.5 x ULN (5). Total bilirubin greater than 1.6 unless history of Gilbert's disease (6). Serum albumin less than 3.0 g/dL (7). INR greater than 1.7 unless subject has stable INR on anticoagulation (8). ALT or AST greater than 350 # - if any of the laboratory exclusion criteria above are met, may have the abnormal value retested one time

2.4 Study Flowchart



- PI will meet with each patient who is eligible
- Hep C antibody and PCR RNA positive

- Meet inclusion and exclusion criteria

- Hep C genotyping
- Hep C viral load
- LFT, PT, INR, PTT, HepBsAg, HIV
- Fibroscan or Liver Biopsy
- NS5A testing (genotype 1a)

- Single visit
- Subsequent visit for cirrhosis management or cancer surveillance

- Genotype 1 a, Rx Naïve, NS5A Neg : GZR 100 mg / EBR 50 mg QD x 12 wk
- Genotype 1 a, Rx Naïve, NS5A Pos : GZR 100 mg / EBR 50 mg + Ribavirin 16 wk
- Genotype 1 b, Rx Naïve : GZR 100 mg / EBR 50 mg QD x 12 wk
- Genotype 1 a or 1 b – Prior Rx PEGINF/Ribavirin or DAA: GZR 100 mg / E Ribavirin 200 mg QD x 12 wk
- Genotype 4, Rx Naïve : GZR 100 mg / EBR 50 mg QD x 12 wk
- Genotype 4, Prior Rx : GZR 100 mg / EBR 50 mg + Ribavirin 200 mg QD x

- LFT and RNA viral load at wk 4 (Child's A only), 8, 12. For patient 16 wk wk 16
- If on Ribavirin, Hg q wk; otherwise q 4 wk
- AE and compliance evaluation at 4, 8, 12 wk. For patient 16 wk Rx, also
- Hep C Viral load at 12 weeks post study

2.5 Study Procedures

1. Patients who meet inclusion criteria and do not have exclusion criteria will have their clinical records reviewed by a hepatologist experienced in treatment of hepatitis C . Patients will only receive treatment with Zepatier if the hepatologist review determines them to be eligible for this study. The hepatologist during initial record review will also determine if the patient requires an in-person meeting with the hepatologist pre or post Zepatier treatment

2.. Patients who meet inclusion criteria and do not have exclusion criteria will be assigned treatment with Zepatier with or without Ribavirin according to following schedule:

a. **Drug Dosing**
   (1). Zepatier : 100 mg grazoprevir and 50 mg elbasvir combination – one tablet per day
   (2). Ribavirin – 200 mg per day
b. **Drug Schedule**
   (1).Genotype 1a – treatment naïve without baseline NS5A polymorphisms – Zepatier alone for 12 weeks
   (2). Genotype 1a – treatment naïve with baseline NS5A polymorphisms – Zepatier and Ribavirin for 16 weeks
   (3). Genotype 1b – treatment naïve – Zepatier 12 weeks

(4). Genotype 1a or 1b – prior treatment with PegIFN/RBV and/or HCV NS3/4A protease inhibitor – Zepatier and Ribavirin for 12 weeks
(5). Genotype 4 – treatment naïve – Zepatier for 12 weeks
(6). Genotype 4 – prior treatment – Zepatier and Ribavirin for 16 weeks

3. . Subjects will be instructed to take Zepatier + ribavirin at bedtime. Phosphate binders should be taken at least 3 hours before or 3 hours after taking the Zepatier + ribavirin. If a subject misses a dose of Zepatier + ribavirin and it is less than 8 hours before the next dose, the missed dose should be skipped and the normal dosing schedule resumed. Subjects should not double the next dose to compensate for the missed dose.

4.. Subjects may withdraw consent at any time for any reason or be dropped from the trial at the discretion of the investigator should any untoward effect occur.

5.. Subject will be discontinued from treatment for any of following:
a. Becomes pregnant during trial
b. Investigator feels it is in best interest of subject to discontinue such as SAE which investigator feels if possibly or probably related to study medication.
c. Abnormal LFT develop: if ALT increases to greater than 10x ULN and persistently remains greater than 10x ULN. Discontinuation as well if ALT elevation is accompanied by signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or INR.

6.. Role of Clinical Pharmacologist
a. Confirming all patients meet inclusion and exclusion criteria
b. Reviewing patient medications to identify medications which prevent participation or which require specific dosage adjustments or monitoring during the study
c. Ensuring that all baseline studies have been performed and the results are entered into the clinical case record
d. Schedule and review with PI all ongoing monitoring labs during active treatment
e. Schedule and review with PI all post treatment monitoring labs
f. Dispense Zepatier alone or with Ribavirin depending on presence or absence of polymorphism or prior treatment
g. Monitor study participants for compliance with study medication
h. Monitor study participants for any adverse events, record such adverse events in the clinical case record and determine

with the physician investigators if the study events are drug related

i. Obtain third-party approval for payment of study drugs

7.. Additional baseline/screening testing:

a. Hepatitis C genotype testing

b. Hepatitis C viral RNA load

c. Liver function tests

d. Protime (PT), INR, and Partial Thromboplastin Time (PTT)

e. HIV test – if positive determine if virus free on HAART, viral RNA load, and CD4 and T cell count

f. Liver biopsy (within 24 months of treatment) or Fibroscan (within 12 months of treatment)

g. History of alcohol use and alcohol testing when relevant

h. *Hepatitis BsAg and HepB cor Ab test - if the Hep BsAg or the Hep Bcore ab is positive, then obtain HBVdna at weeks 4, 8, 12 of therapy and at SVR12 post therapy*

i. For patients with Hepatitis genotype 1a, additional testing to determine if NS5A mutation is present or absent.

j. For patients with a history of intravenous or alcohol abuse, documentation will be needed to demonstrate that a discussion occurred with the patient discussing the risks of substance abuse and that the provider has offered to get substance abuse help for the patient

k. Additional baseline/screening testing/information will be obtained if requested by a third-party payer as a requirement for drug approval

l. Review of the clinical records for all candidate patients with a hepatologist or infectious disease physician with expertise in hepatitis C management before treatment is initiated to review all laboratory and clinical history data. At this review, there will be a determination of the fibrosis stage, including the presence or absence of cirrhosis and to guide optimal choice of therapy as well as determine if there is a need for long term cirrhosis management and liver cancer surveillance. In-personoffice visits with this physician will be determined on presence/absence of cirrhosis and otherwise on an as needed basis as determined by the dialysis nephrologist or hepatologist.

m. Treatment of HIV/HCV co-infected patients will need to be done in collaboration with the patient's primary HIV provider prior to starting and during HCV therapy to determine if any adjustments to the HIV regimen will need to be undertaken:

(1). Zepatier can be used with antiretroviral drugs which do not have significant interactions with Zepatier : abacavir, emtrictabine, enfuvirtide, lamivudine, raltegravir, doloutegravir, rilpivirine, and tenovir. Other antiretroviral drugs allowed will be determined based on package insert, consultation with specialty

	pharmacists, and the HIV treating physician Source - http://www.hcvguidelines.org/full-report/unique-patient-populations-patients-hivhcv-coninfection (2). In patients who are taking warfarin, Protime and INR values will be obtained weekly during and following the study to determine if there are any alterations in the Protime and INR due to a Zepatier-Warfarin interaction. Any alterations will result in warfarin dosage adjustments to achieve therapeutic anticoagulation as measured by Protime and INR 8. . Testing/Evaluations During Active Treatment a. Liver function tests and RNA viral load at week 4 (only in patients with Child's A cirrhosis), 8, and 12 of treatment. For patients on 16 week therapy, LFT also at week 16. b. In patients who are treated with combination of Zepatier and Ribavirin, hemoglobin monitoring every week during course of treatment c. Clinical Pharmacology evaluation for compliance and adverse events at week 4, 8, and 12 (and week 16 for patients receiving a 16 week treatment course). 9.. Testing/Evaluation Post Treatment a. RNA viral load at 12 weeks post treatment b. Clinical Pharmacology evaluation 12 weeks post treatment for adverse events and determination if a SVR was achieved at 12 weeks post treatment c. Patients who have a SVR at 12 weeks will be identified in the hemodialysis treatment records as hepatitis C ab positive but hepatitis C viral RNA PCR negative
2.6 Study Duration	It is estimated all subjects will be recruited and complete treatment over a 9 to 12 month period of time
2.7 Statistical Analysis and Sample Size Justification	The co-principle investigators Dr. Michael R. Rudnick and Dr. Deirdre Sawinski will be responsible for analyzing all data Since this study does not have a control or comparator group, issues of blinding are non-applicable <u>Statistical Methods</u> The planned primary analysis will be the proportion of patients who following treatment have achieved a SVR at 12 weeks following completion of treatment.

	Secondary analyses will determine (a) proportion of patients for whom third party approval for Zepatier treatment was successfully obtained (b) logistic barriers to getting third party approval (c) adverse events with treatment The design of this protocol does not require any specific statistical methods to test the hypothesis <u>Power/Sample Size:</u> A sample size to determine adequate statistical power is not applicable to this protocol since there is only one treatment group and the outcome is binary (SVR at 12 weeks achieved or not achieved) . However, the sample size of approximately 30 patients chosen for this study will be adequate to test the hypothesis and meet the objectives of this study
2.8 Specific Drug Supply Requirements	Study drugs Zepatier and Ribavirin will be provided by Merck free of charge to all study participants. Grant support from Merck will also cover the expenses of any laboratory testing which is routine and not covered by the participant's health insurance Study drugs should be provided to investigator by bulk supplies from Merck and investigators pharmacy (Penn Presbyterian Medical Center) will be responsible for filling individual patient containers and labeling the containers . Blindng of study drugs will not be required in this study. Clinical supplies will be packaged and labeled according to policies and procedures of the Pharmacy Department of the University of Pennsylvania Health System At conclusion of the study or upon drug expiration, the MSD GRS will be responsible for issuing a Drug Disposition Letter to the investigator for US based studies. The investigator will be responsible for the destruction of the supplies at the study center pursuant to the ICH/GCP Guidelines, local regulations and the investigator's institutional policies. Clinical supplies will be received by Pharmacist Amanda Brinkley (designated person) at the study site, and will be handled and stored safely and properly, and kept in a secured location (Penn Presbyterian Pharmacy) to which only the investigator and Amanda Brinkley have access. Clinical supplies will be dispensed in accordance with the protocol. Accurate records will be kept of

	the clinical supplies, the amount dispensed to and returned by the patients, and the disposition at the end of the study.
2.9 Adverse Experience Reporting	The investigator agrees to follow the requirements for adverse experience reporting outline in the study agreement. In addition to following the study agreement requirements for adverse experience reporting, this study will monitor and address any adverse experience as follows: 1.Patient's adverse events will be recorded at the time of spontaneous reporting during the period of active drug treatment 2.In addition, patients will be queried about adverse events at weeks 4,8, and 12 and in those cases with extended treatment, at week 16 3.The principal investigator or sub-investigator (physician or clinical pharmacologist) will determine the severity and relationship to study medication(s) of all adverse events. A physician investigator will review, initial, and date the severity of all adverse events and their relationship to study medications when initial assessment of an adverse event is made by the clinical pharmacologist 4.An adverse event is defined as any untoward medical occurrence in a patient administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An adverse event can be any unfavorable and unintended sign or lab result, symptom, or disease temporally associated with the use of Zepatier or Ribavirin whether or not considered related to use of these products. Any worsening of a pre-existing condition that is temporally associated with the use of Zepatier or Ribavirin is also an adverse event 5.All adverse events will be recorded from the time the consent form is signed through 14 days following cessation of treatment and at each 4 week evaluation during the active treatment phase on an Adverse Event case report form 6.Although pregnancy and lactation are not considered adverse events, the investigators will report any pregnancy or lactation in any of the treated subjects including the pregnancy of a male subject's female partner that occurs during the trial and for 6

	months following completion of treatment regardless if Zepatier was used alone or in combination with Ribavirin 7.Any serious adverse event will be reported within 24 hours to the sponsor in accordance with policies of Merck. All serious adverse events will be followed up for outcome. Serious adverse events are those that (a) result in death (b) life threatening (c) result in persistent or significant disability (d) result in or prolongs an existing hospitalization (e)congenital anomaly or birth defect (f) is a cancer (g)is associated with an overdose (h)is another important medical event
2.10 Itemized Study Budget	A preliminary budget has been previously submitted as a separate attachment and does not require revision with this resubmission of the protocol
2.11 References	1.Webster DP, Klenerman P, Dusheiko G. Hepatitis C. Lancet 2015; 385: 1124-1135 2.Ladino M, Pedraza F, Roth D. Hepatitis C virus infection in chronic kidney disease. J Am Soc Nephrol 2016; 27: 3.Roth D, Gaynor JJ, Reddy R, Ciancio G et al. Effect of kidney transplantation on outcomes among patients with hepatitis C. J Am Soc Nephrol 2011; 22:1152-1160 4.Fabrizi F, Martin P, Messa P. New treatment for hepatitis C in chronic kidney disease, dialysis, and transplant. Kidney Int 2016; 89:988-994 5.Kalantar-Zadeh K, Kilpatrick RD, McAllister CJ, Miller LG, et al. Hepatitis C virus and death risk in hemodialysis patients. J Am Soc Nephrol 2007; 18:1584-1593 6.Carvalho-Filho RJ, Feldner AC, Silva AE, Ferraz ML. Management of hepatitis C in patients with chronic kidney disease. World J Gastroenterol 2015; 21:408-422 7.Sawinski D and Bloom RD. Novel hepatitis C treatment and the impact on kidney transplantation. Transplantation 2015; 99: 2458-2466 8.Roth D, Nelson DR, Bruchfeld A, Liapakis A, et al. Grazoprevir plus elbasivir in treatment-naïve and treatment experienced patients with hepatitis C virus genotype 1 infection and stage 4-5

	chronic kidney disease (the C-SURFER study): a combination phase 3 study. Lancet 2015; 386:1537-1545 9.Jadoul M and Horsmans Y. Towards eradication of hepatitis C virus from dialysis units. Lancet 2015; 386:1514-1515 10.Brennan BJ, Wang K, Blotner S, Magnusson MO, et al. Safety, tolerability, and pharmacokinetics of ribavirin in hepatitis C virus-infected patients with various degrees of renal impairment. J Antimicrob Chemother 2013; 57:6097-6105 11.Khakuk A, Mujtaba MA, Aljanabi O, Ghabril MS, Taber TE, Yaqub MS, Sharfuddin A. Exper Clin Transplant 2015 (e-pub) 12.http://www.hcvguidelines.org/full-report 13.Kidney Disease: Improving Global Outcomes. KDIGO clinical practice guidelines for the prevention, diagnosis, evaluation, and treatment of Hepatitis C in chronic kidney disease. Kidney International 2008; 73 (Suppl 109): S1–S99.
2.12 Publication Plan	1.It is our intent to use the results of this study to publish an article directed towards Nephrologists and hemodialysis personnel to provide guidelines and a strategic protocol for use of DAAs like Zepatier with the goal of eradicating hepatitis C in a dialysis population 2. The study is expected to take between 9 to 12 months. Another 3 to 6 months will be required at study completion to submit a manuscript for publication 3. The specific journal to which the manuscript will be submitted has not yet been determined but given that the study's audience is nephrologist, a Nephrology specialty journal is most likely. Suggestions would include Clinical Journal of the American Society of Nephrology, Kidney International, Seminars in Dialysis, and Nephrology, Dialysis, and Transplantation 4.The publication of abstracts and presentation at meetings has not yet been determined 5. All of the investigators listed in this protocol will be co-authors. This group will elect a small writing group whose responsibility

	will be to provide the initial draft and then revisions after review and discussions by the larger group **6.The investigators of this protocol are not opposed to publication collaboration with members of Merck's hepatitis C scientific team**
2.13 Curriculum Vitae	**Submitted as a separate attachment**
2.13 Protocol Submission for Investigator-Initiated Studies	U.S. protocols should be submitted by US investigators directly or through the Global Research Specialist at www.merckiisp.com Non U.S. protocols should be submitted to the MSD office by the investigators.

Study Procedures

Hepatitis C antibody testing is performed routinely as per unit protocol for the clinical care of dialysis patients. These standard of care labs will be reviewed and Hepatitis C antibody positive patients identified. Patients will have a Hepatitis C viral load and genotype performed. Patients who are viral load positive and genotype 1 or 4 will be eligible to participate and approached about the study.

	Visit 0	Visit 1	Visit 2	Visit 3-5	Visit 6
Study week	prescreening	enrollment	1	4,8,12	24
Review HCV Ab results	X				
HCV viral load and genotype	X				
Sign informed consent		X			
NS5a testing		X (genotype1 only)			
LFTs, PT, PTT, INR, Hepatitis B, HIV		X			
Fibroscan or review of liver biopsy		X			
Referral to Hepatology		X (only for patients with cirrhosis)			
Referral to ID		X (only for patients with HIV)			
Review by Transplant Nephrology		X (evaluate potential for transplant, review listing status)			
Apply for Insurance approval		X			
Start study drug			X		
LFTs			X	X	
HCV VL			X	X	X
Hemoglobin			X (only if on Ribavirin)	X (only if on Ribavirin)	
Adverse event assessment				X	
Compliance assessment				X	

Patients who consent to participate will have a NS5A polymorphism checked in order to determine if Ribavirin administration is required. Study drug(s) will be administered as follows:

Genotype	NS5A	Prior treatment	Drug(s)	Duration
1a	no	no	Zepatier	12 weeks
	yes	no	Zepatier + Ribavirin	16 weeks
	no	yes	Zepatier + Ribavirin	12 weeks
1b	n/a	no	Zepatier	12 weeks
	n/a	yes	Zepatier + Ribavirin	12 weeks
4	n/a	no	Zepatier	12 weeks
	n/a	yes	Zepatier + Ribavirin	16 weeks

Subjects will be instructed to take Zepatier + ribavirin at bedtime. Phosphate binders should be taken at least 3 hours before or 3 hours after taking the Zepatier + ribavirin. If a subject misses a dose of Zepatier + ribavirin and it is less than 8 hours before the next dose, the missed dose should be skipped and the normal dosing schedule resumed. Subjects should not double the next dose to compensate for the missed dose.

Subjects may withdraw consent at any time for any reason or be dropped from the trial at the discretion of the investigator should any untoward effect occur.

Subject will be discontinued from treatment for any of following:

a. Becomes pregnant during trial

b. Investigator feels it is in best interest of subject to discontinue such as SAE which investigator feels if possibly or probably related to study medication.

c. Abnormal LFTs develop: if ALT increases to 10x upper limit of normal and persistently remains 10x upper limit of normal. Discontinuation as well if ALT elevation is accompanied by signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or INR.

Role of Clinical Pharmacologist

a. Confirming all patients meet inclusion and exclusion criteria

b. Reviewing patient medications to identify medications which prevent participation or which require specific dosage adjustments or monitoring during the study

c. Ensuring that all baseline studies have been performed and the results are entered into the clinical case record

d. Schedule and review with PI all ongoing monitoring labs during active treatment

e. Schedule and review with PI all post treatment monitoring labs

f. Dispense Zepatier alone or with Ribavirin depending on presence or absence of polymorphism or prior treatment

g. Monitor study participants for compliance with study medication

h. Monitor study participants for any adverse events, record such adverse events in the clinical case record and determine with the physician investigators if the study events are drug related

i. Obtain third-party approval for payment of study drugs

Additional baseline/screening testing:

a. Hepatitis C genotype testing

b. Hepatitis C viral RNA load

c. Liver function tests

d. Protime (PT), INR, and Partial Thromboplastin Time (PTT)

e. HIV test: if positive determine if viral load negative on HAART, viral RNA load, and CD4 and T cell count

f. review liver biopsy (within 24 months of treatment) or Fibroscan (within 12 months of treatment)

g. History of alcohol use and alcohol testing when relevant

h. Hepatitis BsAg and HepB core Ab test - if the Hep BsAg or the Hep Bcore ab is positive, then obtain HBV DNA at weeks 4, 8, 12 of therapy and at SVR12 post therapy

i. For patients with Hepatitis genotype 1a, additional testing to determine if NS5A mutation is present or absent.

j. For patients with a history of intravenous or alcohol abuse, documentation will be needed to demonstrate that a discussion occurred with the patient discussing the risks of substance abuse and that the provider has offered to get substance abuse help for the patient

k. Additional baseline/screening testing/information will be obtained if requested by a third-party payer as a requirement for drug approval

l. One office visit for all candidate patients with a hepatologist or infectious disease physician with expertise in hepatitis C management before treatment is initiated to review all laboratory and clinical

history data. At this visit, there will be a determination of the fibrosis stage, including the presence or absence of cirrhosis and to guide optimal choice of therapy as well as determine if there is a need for long term cirrhosis management and liver cancer surveillance. Further office visits with this physician will be determined on presence/absence of cirrhosis and otherwise on an as needed basis as determined by the dialysis nephrologist.

m. Treatment of HIV/HCV co-infected patients will need to be done in collaboration with the patients primary HIV provider prior to starting and during HCV therapy to determine if any adjustments to the HIV regimen will need to be undertaken:

(1). Zepatier can be used with antiretroviral drugs which do not have significant interactions with Zepatier : abacavir, emtrictabine, enfuvirtide, lamivudine, raltegravir, doloutegravir, rilpivirine, and tenovir. Other antiretroviral drugs allowed will be determined based on package insert, consultation with specialty pharmacists, and the HIV treating physician

Source - http://www.hcvguidelines.org/full-report/unique-patient- populations-patients-hivhcv-coninfection

Testing/Evaluations During Active Treatment

a. Liver function tests and RNA viral load at week 4 (only in patients with Childs A cirrhosis), 8, and 12 of treatment. For patients on 16 week therapy, LFT also at week 16.

b. In patients who are treated with combination of Zepatier and Ribavirin, hemoglobin monitoring every week during course of treatment

c. Clinical Pharmacology evaluation for compliance and adverse events at week 4, 8, and 12 (and week 16 for patients receiving a 16 week treatment course).

Testing/Evaluation Post Treatment

a. RNA viral load at 12 weeks post treatment

b. Clinical Pharmacology evaluation 12 weeks post treatment for adverse events and determination if a SVR was achieved at 12 weeks post treatment

c. Patients who have a SVR at 12 weeks will be identified in the hemodialysis treatment records as hepatitis C ab positive but hepatitis C viral RNA PCR negative

Log out

Basic Info | Personnel | [illegible] | Sponsors | Sites | Protocol | Populations | Procedures | Consent | Risk/Benefit | Confirmation

Protocol Form - Miscellaneous

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Clinical Trial*

Is this a clinical trial? Please note the following definition:

- Clinical trial is defined as a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes. See CFR 45.46.102(b)

Yes

If Yes, please be aware that for each clinical trial conducted or supported by a Federal department or agency, one IRB-approved informed consent form used to enroll subjects must be posted by the awardee or the Federal department or agency component conducting the trial on a publicly available Federal Web site that will be established as a repository for such informed consent forms.

Investigator Initiated Trial*

Is this an investigator initiated trial? Please select "Yes" if ALL the following conditions are met:

- The research is subject to FDA regulations for human subjects research.
- The individual PI both initiates (plans and designs) and conducts an investigation and under whose immediate direction the investigational agent is administered or dispensed. The individual investigator has absolute responsibility and accountability and designs, conducts, monitors, manages the data, prepares reports and oversees all regulatory and ethical matters. See 21 CFR 312.3

Yes

If Yes, please be aware that the investigator may be required to create and manage a record of this trial in **https://clinicaltrials.gov**.

Drugs or Devices*

Yes: Drugs, products or devices are used in accordance with FDA approval.

For studies including IND or IDE's, please provide the number(s) below

IDE Review*

NOTE: For research involving investigational devices, you are required to review the guidance on Managing Research

Device Inventory.

Consult the Penn Manual for Clinical Research:

https://somapps.med.upenn.edu/pennmanual/secure/pm/investigational-product-management-sites-not-using-investigational-drug-services-ids

Please check the box Yes if you have reviewed the guidance.
Yes

Research Device Management*

Please indicate how research device(s) will be managed.
Not Applicable (no investigational devices)

Drug, Herbal Product or Other Chemical Element Management *

Please indicate how drugs, herbal products or other chemical entities will be managed.
Not Applicable (no drugs, herbal products or other chemical entities)

Radiation Exposure*

Are research subjects receiving any radiation exposure (e.g. X-rays, CT, Fluoroscopy, DEXA, pQCT, FDG, Tc-99m, etc.) that they would not receive if they were not enrolled in this protocol?

- IF YES, the protocol must be approved by the Radioactive Drug Research Committee. Consult EHRS web site: **www.ehrs.upenn.edu/protocols/radiohuman.html** for submission requirements.
- If you have questions, call 215-898-7187.

No

Gene Transfer*

Does this research involve gene transfer (including all vectors) to human subjects?

- IF YES, the protocol must be approved by the Institutional Biosafety Committee. Consult EHRS web site: www.ehrs.upenn.edu/protocols/bio_humans.html for submission requirements
- If you have questions, call 215-898-4453.
- The protocol may also require review by the Senior Vice Provost for Research's Human Research Advisory Committee(HRAC). The IRB will notify the PI and study staff if this review is warranted.

No

Human Source Material*

Does this research include collection or use of human source material (i.e., human blood, blood products, tissues or body fluids)?

- IF YES, consult the EHRS web site: **www.ehrs.upenn.edu/programs/bio/bbpathogens.html** for information on OSHA Bloodborne Pathogens requirements (training, vaccination, work practices and Exposure Control Plan).
- If you have questions, call 215-898-4453.

No

CACTIS and CT Studies*

Does the research involve Center for Advanced Computed Tomography Imaging Services (CACTIS) and CT studies that research subjects would not receive if they were not part of this protocol?

- IF YES, consult CACTIS website: **http://www.uphs.upenn.edu/radiology/research/labs/cactis/** for application requirements

No

CAMRIS and MRI Studies*

Does the research involve Center for Advanced Magnetic Resonance Imaging and Spectroscopy (CAMRIS) and MRI studies that research subjects would not receive if they were not part of this protocol?

- IF YES, consult CAMRIS website: **http://www.med.upenn.edu/cbi/camris-home.html** for application requirements

No

Investigational Agent or Device within the Operating Room*

Does the research project involve the use of an investigational agent or device within the Operating Room?

- IF YES, contact Associate Executive Director, Surgical Services: (215) 662-2089

No

Cancer Related research not being conducted by an NCI cooperative group*

Does this protocol involve cancer-related studies in any of the following categories?

Therapeutic, Prevention, Supportive Care, Screening, Early Detection, or Diagnostic, Epidemiologic, Observational, Outcome, Ancillary or Correlative.

For a description of these categories, see **http://www.ctsrmc.org/submitting_a_protocol.php**

NCI Cooperative Groups are as follows:

Alliance for Clinical Trials in Oncology	**NCI Clinical Trials Group (Canadian Cancer Society) (NCCTG)**
Children's Oncology Group (COG)	**NRG Oncology Group**
ECOG-ACRIN Cancer Research Group	**Southwest Oncology Group (SWOG)**

- IF YES, the protocol must be submitted to the Cancer Center's Clinical Trials Scientific Review Committee for scientific review and approval prior to obtaining IRB approval. Consult the CTSRMC website: **www.ctsrmc.org** for application requirements

No

Processing of Materials*

Will the research involve processing (such as over encapsulating, or compounding)?
No

In-House Manufacturing of Materials*

Will the research involve processing (such as over encapsulating, or compounding)?
No

Medical Information Disclosure*

Does the research proposal involve the use and disclosure of research subject's medical information for research purposes?
Yes

Modified research informed consent document that incorporates HIPAA requirements

CTRC Resources*

Does the research involve CTRC resources?
No

Pathology and Laboratory Medicine Resources*

Will samples be collected by hospital phlebotomy and/or processed or analyzed by any of the clinical laboratories of the University of Pennsylvania Health System?
No

Please confirm analysis is being performed at outside contract laboratories OR confirm that no samples are being collected for research purposes.
** If neither of the above options applies to your research, then please change your answer to the above question. Please confirm analysis is being performed at outside contract laboratories OR confirm that no samples are being collected for research purposes.
** If neither of the above options applies to your research, then please change your answer to the above question.

Research Involves Apheresis, Cell Collection, and/or Blood Product Collection*

Does this research involve collection of blood products in the Penn Donor Center and/or the use of apheresis for treatment or collection of cells or other blood components?
No

Research involving blood transfusion or drug infusions*

Will your research involve blood transfusion or infusion of study drug in 3 Ravdin Apheresis Unit for research purposes?
No

Trial in Radiation Oncology

Is this research a prospective trial being done in Radiation Oncology, and if so, has this protocol been approved by the Radiation Oncology Protocol committee?

N/A

Study in Radiation Oncology

Is this research a retrospective study being done in Radiation Oncology, and if so, has this project been reviewed by the Radiation Oncology Clinical Research Group?

N/A

Use of UPHS services*

Does your study require the use of University of Pennsylvania Health System (UPHS) services, tests or procedures*, whether considered routine care or strictly for research purposes? (UPHS includes all Penn hospitals and clinical practices, including the Clinical Care Associates network of community practices).

*Examples of UPHS services/tests/procedures includes the Clinical Translational Research Center (CTRC), laboratory tests, use of the pathology lab, cardiovascular imaging tests or radiology imaging tests (whether being billed via the Service Center or through UPHS), other diagnostic tests & procedures and associated professional services, etc.

If yes, the following is required:

- Completion and submission of a Prospective Reimbursement Analysis (PRA) to the Office of Clinical Research.
  - There are four PRA Templates: Device, Drug, Non-Drug Device, and Non-Interventional. The links are below:
    - **http://www.med.upenn.edu/ocrobjects/prod/CMS/PRA/PRA_Template_Device.xls**
    - **http://www.med.upenn.edu/ocrobjects/prod/CMS/PRA/PRA_Template_Drug.xls**
    - **http://www.med.upenn.edu/ocrobjects/prod/CMS/PRA/PRA_Template_Non-Drug_Device_Intervention.xls**
    - **http://www.med.upenn.edu/ocrobjects/prod/CMS/PRA/PRA_Template_Non-Intervention.xls**
  - A study budget that differentiates protocol-required UPHS services as routine care vs. research (including CPT codes)
  - Supporting documentation for the routine care determination (if applicable)
  - Study protocol and informed consent form
  - Study contract or notice of grant award (if applicable)

No

Primary Focus*

The **primary** focus of your research is best described by which of the following (single best answer):

Clinical Trial (prospectively assigning subjects to health-related interventions to evaluate outcomes)

Protocol Interventions*

Does your protocol require any of the following interventions? Check all that apply.

Drug

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Send questions or comments about this site to: **hsera_help@lists.upenn.edu** or **hsera_ctrc@lists.upenn.edu** -
Please do not include confidential information in your Email.

Log out

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Protocol Form - Sponsor

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Business Administrator***

***The Department of Medicine requires the inclusion of a Business Administrator (BA) for all regulatory submissions.

Name	PATTERSON, LAMORIA
Department/School/Division	4423 - PS-Mental Health Services
Phone	317-654-5682
Fax	215-746-2988
Pager	
Email	lamoria.patterson@pennmedicine.upenn.edu

Department budget code

000- 0000 - 0 - 000000 - 0000 - 0000 - 0000

Funding Sponsors

Name	MERCK & CO., INC.
Type	UPENN Commercial/Industrial

Funding sponsors billing address

If you have selected a commercial or industry sponsor, please provide the appropriate address and contact information for the Sponsor for the purposes of billing for IRB review fees (initial review, continuing review and convened modification fees apply here). If the Sponsor is not industry/commercial, this information is not necessary to provide with your application.

Funding sponsors gift

Is this research being funded by a philanthropic gift?
No

If the answer to this question is "yes", University Policy requires that the gift agreement signed by the donor includes a disclosure that iterates an individual gift may not fund a specific research protocol on which they or their family member

wishes to participate. Please contact the Director of the IRB, Tracy Ziolek (ziolekt@upenn.edu or 215-746-6272) if you have any questions.

Please note: If the initial answer to this question is "no", but a gift is received during the conduct of this research study, the answer must be updated to "yes" upon receipt of the gift.

Regulatory Sponsor

Name
Type

IND Sponsor

Name
Department/School/Division
Phone
Fax
Pager
Email

Industry Sponsor

Sponsor Name

Contact Name

Street Address

Street Address (continued)

City, State/Province, Zip/Postal Code

Phone Number

Fax Number

Email Address

CRO Name

CRO Contact Person

CRO Street Address

CRO Street Address (continued)

CRO City, State/Province, Zip/Postal Code

CRO Phone

CRO Fax

CRO Email

Send bills for IRB to

Project Funding*

Is this project funded by or associated with a grant or contract?
Yes

Proposal Number	Title
10063958	"Real World" Administration of Zepatier (Grazoprevir plus Elbasvir) in Chronic Hemodialysis Patients

You are required to submit a copy of the grant, minus appendices, for review by the IRB.

Funding Application

There are no documents attached for this item.

Sponsor Funding

Is this study funded by an industry sponsor?
Yes

The University of Pennsylvania IRB charges fees to industry sponsors to cover the costs associated with the IRB's review and related administrative responsibilities. No fees are charged for studies funded by grants, non-profits, or internal funding.

For further information regarding the IRB Fee Policy, please visit:
http://www.upenn.edu/regulatoryaffairs/index.php?option=com_content&task=view&id=19&Itemid=8

Status of contract

Complete

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Please do not include confidential information in your Email.

Log out

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Protocol Form - Multi-Site Research

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Site Information

Management of Information for Multi-center Research where a Penn Investigator is the Lead Investigator of a multi- center study, or Penn is the lead site in a multi-site study. Provide a plan for the management of multi-site information that may be relevant to the protection of human research participants, such as:

- Reporting unanticipated problems involving risks to participants or others.
- Reporting of interim results.
- Coordination of protocol modifications.

PLEASE NOTE: This information must be included if Penn is the lead/data coordinating site.

There are no documents attached for this item.

Other Sites

Other Sites participating in the study

Management of Information for Multi-Center Research

- Reporting unanticipated problems involving risks to participants or others.
- Reporting of interim results.
- Coordination of protocol modifications.

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Protocol Form - Details of Protocol

Abstract

We propose a "real world" observational study of Hepatitis C treatment in a cohort of prevalent dialysis patients. We will study response to therapy in the "real world" setting and identify barriers to treatment.

Objectives

Overall objectives

The primary objective is to develop real world strategies for the successful treatment of hepatitis C hemodialysis patients using Zepatier in a hemodialysis unit with a high prevalence of hepatitis C to improve patient outcomes and to reduce the risk of in-facility transmission of hepatitis C. These strategies developed will be primarily directed to Nephrologists and Hemodialysis Personnel (Nurses, Social Workers, Dieticians) in order that these individuals will gain the knowledge to administer a hepatitis C eradication program using Zepatier in their hemodialysis centers

Primary outcome variable(s)

The specific real world measures to be developed and summarized in this protocol are:
a. Identify hepatitis C patients who meet the virologic and medical criteria for treatment with Zepatier alone or in combination with ribavirin
b. Identify necessary pretreatment clinical and laboratory assessments that are needed before initiating treatment with Zepatier.
c. Identify appropriate treatment candidates.
d. Identify clinical and laboratory testing to monitor during treatment.
e. Perform post-treatment testing of sustained virologic response to treatment (SVR at 12 weeks).

Secondary outcome variable(s)

Secondary outcomes include:
-Identifying steps required to obtain 3rd party insurance approval
-Identify barriers to third-party payment of treatment and steps necessary to overcome these barriers.
-Identify the roles of a clinical pharmacologist and non-physician health care personnel such as a dialysis nurse, social worker, and dietician in a Zepatier treatment protocol of hepatitis C infected dialysis patients.
-Identify available patient assistance programs for drug obtainment and criteria needed to qualify for such assistance.

Background

Hemodialysis patients have an exceptionally high prevalence of hepatitis C, with prevalence rates up to 25% in urban hemodialysis units in the United States and greater than 50% in less developed countries. It has been estimated that by 2020, 775,000 patients with ESRD will need dialysis in the United States and 109,000 of these patients will be infected with hepatitis C. Hepatitis C is associated with an increased mortality among hemodialysis patients with a relative risk of 1.59 (95% CI, 1.33- 1.86). Kidney transplant recipients with hepatitis C also have an increased mortality with a relative

risk of 1.79 (95% CI. 1.57-2.03). In addition hepatitis C infected transplant patients have an increased death rate from infection in the early (6 months) post-transplant period and a decreased graft survival. Attempts to prevent nosocomial transmission of hepatitis C in dialysis units by implementing universal precautions have not been consistently successful. The introduction of direct acting antivirals (DAAs) in 2011 as a treatment of hepatitis C patients has created a paradigm treatment shift for these patients. The DAAs have been shown to be highly effective with SVR rates greater than 90 to 95% in treatment naïve hepatitis C infected patients in the general population.One DAA, Zepatier is well suited for treatment of hemodialysis patients as well as patients with stage 4 or 5 chronic kidney disease not requiring hemodialysis since less than 1% of this DAA is excreted by the kidney. A recent randomized double-blind multicenter study compared Zepatier to placebo in stage 4 and 5 chronic kidney disease patients most of whom were hemodialysis dependent (77%) and who had infection with hepatitis C genotype 1. A SVR at 12 weeks after the end of therapy was achieved in 99% of patients who received Zepatier.

The majority of hemodialysis patient care is provided by nephrologists and hemodialysis healthcare personnel. Both of these caregiver groups have become quite adept at providing protocol driven medical care uniquely suited to this population and care setting. Although hemodialysis patients often have primary care providers and other medical specialists who participate in their care, dialysis patients are often reluctant to see these non-Nephrology physicians due to their demanding dialysis schedule. Furthermore, non-Nephrology providers often feel uncomfortable providing care and prescribing medications to patients with severely impaired renal function. Thus, nephrologists and hemodialysis personnel are uniquely situated to implement and monitor treatment protocols using DAAs such as Zepatier in dialysis unit patients with hepatitis C infection. Clear and current guidelines for the implementation and monitoring of DAA treatment protocols in the hemodialysis population currently do not exist, and the development of such guidelines is one of the purposes of this protocol. While nephrologists and hemodialysis health care personnel are aware of the prevalence of hepatitis C in hemodialysis patients and that DAAs are now available for treatment of such patients, most nephrologists and hemodialysis personnel are not aware of the specific real world steps required to identify and treat such patients

One aim of our study is to provide the specific real world steps which must be taken to successfully treat hepatitis C hemodialysis patients with DAAs. Application of these steps will allow hemodialysis units to implement guidelines which will allow DAA treatment of all eligible patients in a timely manner, thus reducing or eliminating the health consequences of hepatitis C infection is this special population. This real world protocol will be developed and implemented by a diverse group of investigators, each with a unique area of expertise needed for such a protocol development with real world implementation. Members of the investigative team include physicians with expertise in nephrology, hepatology, infectious disease, infection control, transplant nephrology and non-physician personnel with expertise in clinical pharmacology and hemodialysis social services.

Study Design

Phase*
Phase IV

Design
This is a prospective, non-randomized, non-blinded interventional trial of treatment of Hepatitis C with Zepatier.

Study duration

- Estimated length of time to enroll all subjects and complete the study
- Length of a subject's participation time in study
- Project date of the proposed study

We estimate this study will take no more than 1 year to complete. We have already identified all of the Hepatitis C antibody positive patients in the dialysis unit via routine clinical screening for Hepatitis C performed for standard of care dialysis center protocol. We anticipate study participants will require 9 months to complete the study. We anticipate it will take up to 3 months to obtain all of the necessary laboratory results and insurance approvals to obtain Zepatier. Patients will be treated for 12-16 weeks depending on resistance testing results. We will then follow the patients for 12 weeks after the completion of therapy to prove they have achieved a sustained viral response (SVR) or cure.

Resources necessary for human research protection

The investigator will retain copies of CRFs (or electronic files), and source documents for the maximum period required by the country in which the study will be conducted, or the period specified by the Sponsor, whichever is longer. If the investigator withdraws from the study (e.g., relocation, retirement), the records should be transferred to a mutually agreed upon designee (e.g., another investigator, IRB). Notice of such transfer will be provided in writing to the sponsor. Patients have access rights to their data and the possibility to rectify the data according to local law and procedures. They can discuss this issue further with the PI or by direct inquiries to the local data privacy officer representative of the sponsor. We have adequate number of coordinators with many years of experience in clinical trials. They have completed the CITI Patient-Oriented Research Certification program, HIPPA training, and the Health and Radiation Safety (EHRS) training program as well as attending Human Subject Research workshops and the Clinical Research Coordinators (CRC) Forums. It is the site's responsibility to ensure the patients data remains confidential. There will be no secondary use of the data. The only way data will be used is the way described in protocol. In all the data recordings a code will replace the patients name. All the data collected will be kept confidential. The sponsors authorized personnel will enter the data in a computer database. Members of health authorities, the University of Pennsylvania Institutional Review Board or other persons required by law may review the data provided. This data may also be used in publications about the study drug. However, patients identity will not be revealed in any compilations, study reports or publications. Representatives from the sponsor, sponsor affiliates, health authorities and the IRB/IEC may access patients medical records. Such checks will only be done by qualified and authorized personnel. All such persons are required to and will keep the data confidential.

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Protocol Form - Characteristics of the Study Population

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Target population
All prevalent adult hemodialysis patients with genotype 1 or 4 hepatitis C infection.

Subjects enrolled by Penn Researchers
30

Subjects enrolled by Collaborating Researchers
0

Accrual
The prinicipal investigator rounds at the dialysis unit where the study will be conducted; thus he encounters potential study participants in the course of routine dialysis patient care.

The planned primary analysis will be the proportion of patients who following treatment have achieved a SVR at 12 weeks following completion of treatment.

Secondary analyses will determine (a) proportion of patients for whom third party approval for Zepatier treatment was successfully obtained (b) logistic barriers to getting third party approval (c) adverse events with treatment

Key inclusion criteria
All potential study participants must be hepatitis C viral load positive in order to enroll. Those who are antibody positive but viral load negative have either spontaneously cleared their infection or else been previously treated with other therapies. Additionally subjects must:
a. Age: Be 18 or greater on day of signing informed consent
b. HCV treatment status must fall into one of following categories (1) Naïve to all anti HCV treatment (2) Prior INF or PEG IFN plus ribavirin treatment failures (null responders, partial responders, relapses) (3) Intolerant to prior INF or PEG-INF plus ribavirin regimen (4) Prior HCV NS3/4A protease inhibitor failures.
c. Not of reproductive potential hemodialysis patient with 12 months of no menses. Women of childbearing potential should use 2 reliable forms of contraception simultaneously during treatment and for 6 months after completion of therapy. This guideline will be applied for both Zepatier treatment alone or when combined with Ribavirin.
d. Males with partners of reproductive potential as long as contraception is used during and for 6 months after completion of therapy. This guideline will be applied for both Zepatier treatment alone or when combined with Ribavirin.
e. Understand the study procedures, alternative treatments available, risks involved with the study, and voluntarily agrees to participate by giving informed written consent.
f. Both men and women will be eligible to participate.

Key exclusion criteria

a. Unable to provide informed consent
b. Currently undergoing active treatment with a direct acting antiviral agent
c. Have previously undergone successful treatment with a direct acting antiviral agent
d. Have moderate or severe hepatic impairment (Child-Pugh B or C)
e. Have evidence of decompensated liver disease manifested by presence or history of ascites, gastric or variceal bleeding, hepatic encephalopathy, or other signs/symptoms of advanced liver disease
f. Co-administration of known Hepatotoxic Drugs including but not limited to
(1) Etofoxine
(2) Isoniazid
(3) Nitrofurantoin
(4) Phenytoin
g. Patients receiving strong CYP3A/P-gp inhibitors, organic acid transporting polypeptide 1B1/3 inhibitors, strong inducers of cytochrome 450 3A (CYP3A), efavirenz, and other drugs which may interact as per Zepatier package insert.
h. Has a history of substance abuse with alcohol, intravenous drugs, psychotropics, narcotics, cocaine use within 1 year of screening or if shorter, is judged by the investigator to be capable of complying with study procedures.
i. Has a history of any condition, pre-study laboratory abnormality, or ECG abnormality or history of any illness which in the opinion of the investigator might confound the results of the study or pose additional risks from the administration of study drugs.
j. Has evidence or history of chronic hepatitis not caused by HCV including but not limited to nonalcoholic steatohepatitis (NASH), drug induced hepatitis, and autoimmune hepatitis.
k. Patients currently on a kidney transplant waiting list who have agreed to accept HCV positive organ offers.
l. All patients currently undergoing kidney transplant evaluation.
m. Laboratory Exclusion values:
(1). Hemoglobin less than 9 g/dL if patient will require concomitant ribavirin therapy
(2). Neutrophils less than 1,500/uL in Caucasians or less than 1,200/uL in Blacks
(3). Platelets less than 70,000/uL
(4). Direct bilirubin greater than 1.5 x ULN (upper limit normal)
(5). Total bilirubin greater than 1.6 unless history of Gilberts disease
(6). Serum albumin less than 3.0 g/dL
(7). INR greater than 1.7 unless subject has stable INR on anticoagulation
(8). ALT or AST greater than 350
- if any of the laboratory exclusion criteria above are met, may have the abnormal value retested one time

Vulnerable Populations*

None of the above populations are included in the research study

There are no documents attached for this item.

Populations vulnerable to undue influence or coercion

We will attempt to enroll equal amounts of male and female patients into each study group. Economically or educationally disadvantaged patients may be enrolled into the trial. However, investigators will not screen specifically for subject socio-economic status. Cognitively impaired persons are not included in this research study. Economically disadvantaged persons, Penn employees and students will not be specifically targeted, but will be pre-screened and invited to participate if they meet all of the inclusion criteria. These subjects will be informed that their participation or lack there-of in no way impacts their current or future employment or student status at Penn.

Subject recruitment*

All patients will be recruited from our own outpatient dialysis practice. Patients are familiar with both their nephrologist and the dialysis unit pharmacist as they are seen by them as part of their standard

dialysis care. The nephrologist will screen the dialysis patient list to obtain current patients who meet the criteria, and review eligible patients with the transplant nephrologist, to ensure they are not a transplant candidate (which is a study exclusion criterion) prior to contacting or approaching the patient. Patients who satisfy the inclusion/exclusion criteria will be considered for participation in this study. During their standard of care dialysis session, subjects may interact with the Principal Investigator, Co-Investigator, study coordinator, and/or attending and fellows. The Investigator and Study Coordinator will discuss the study thoroughly with each patient. All patient questions will be answered and informed consent will be obtained prior to patient entry.

Use the following button to upload sample ***recruitment materials*** (i.e. radio/video scripts, flyers, internet postings, etc.)
For guidance regarding recruitment materials, please see the following link:
http://www.upenn.edu/regulatoryaffairs/Documents/irbgui-4.pdf

There are no documents attached for this item.

Will the recruitment plan propose to use any Penn media services (communications, marketing, etc.) for outreach via social media avenues (examples include: Facebook, Twitter, blogging, texting, etc.) or does the study team plan to directly use social media to recruit for the research?*
No

Subject compensation*

Will subjects be financially compensated for their participation?
No

Summarize any financial compensation that will be offered to subjects, e.g. cash payments, gift card, reimbursement for travel. The amount of compensation may not constitute an undue inducement to participate in the research. A prorated system of financial compensation is required in most circumstances. Provide the schedule for compensation per study visit or session and total amount for entire participation.
n/a

There are no documents attached for this item.

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Protocol Form - Study Procedures

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Suicidal Ideation and Behavior

Does this research qualify as a clinical investigation that will utilize a test article (ie- drug or biological) which may carry a potential for central nervous system (CNS) effect(s)?

- Centeral nervous system(CNS) effect: the ability of a test article to enter into and potentially interact with the central nervoous system (brain and spinal cord).
- Clinical Investigation: Any experiment that involves a test article and one or more human subjects that either is subject to requirements for prior submission to the Food and Drug Adminstration (FDA) under section 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act, or is not subject to the requirements for prior submission to the FDA under these sections of the act, but, the results of which are intended to be submitted later to, or held for inspection by, the FDA as part of an application for a research or marketing permit.

No

Procedures

- Describe study procedures. Include a table or flow chart, if necessary, showing the schedule of the procedures and interactions. It is important to distinguish between inventions that are experimental and carried out for research purposes versus those that are considered standard of care. In addition, routine procedures that are performed soley for research purposes should also be identified.
- Describe the follow-up of subjects and identify any procedures that are performed exclusively for research purposes or performed more frequently than would be clinically indicated (eg: additional x-rays)
- You may upload additional documentation using the **Upload** button below

Since this is a real-world study, all procedures and interactions performed are standard of care in the treatment of dialysis patients with Hepatitis C infection. We will review standard of care Hepatitis C antibody results and follow up any positive results with a Hepatitis C viral load and genotype. Patients who are viral load positive with genotype 1 or 4 infection will be approached about study participation during a standard of care dialysis visit. Patients who consent to the study will have LFTs, Hg, PT, PTT, INR, HIV and Hepatitis B testing performed, these are all the standard laboratory testing required to safely initiate Hepatitis C treatment. We will refer all patients to Hepatology for an evaluation of their fibrosis stage (either by biopsy or fibroscan, at the discretion of the hepatologist); patients who have stage 4 fibrosis (ie cirrhosis) will only be treated in consultation with hepatology. Patients who are HIV co-infected will be referred to infectious disease and their treatment will only be undertaken in consultation with ID. Pharmacy will go through the necessary steps to obtain insurance approval for the medications but all medications will be provided by the study sponsor. Patients will be started on the study drug and have standard of care laboratory tests performed to monitor liver function while on the medication (LFTs and Hepatitis C viral load; hemoglobin will be followed in patients on ribavirin). Once the study drug is completed, patients will have a final Hepatitis C viral load checked 12 weeks after the completion of therapy to document a cure.

The following documents are currently attached to this item:

Procedures (studyprocedures.docx) Date uploaded: 02/27/2018 10:27:30 AM

Deception

No

Are you conducting research outside of the United States? *

No

Analysis Plan

- **Note:** If the statistical methods used are described in the detailed protocol, this section may reference the detailed protocol.

All analyses will be performed using SAS® for Windows statistical software (SAS Institute, Cary, NC) using validated implementations of each application or SAS custom programming. Programs, logs and output will be reviewed for accuracy according to relevant Standard Operating Procedures (SOPs). A full Statistical Analysis Plan will be developed and finalized prior to data base lock. The plan will include a thorough description of the statistical methods to be used to address study objectives. In general, continuous variables will be summarized with number of non-missing observations, mean, standard deviation (SD), median, minimum and maximum displayed. Categorical variables will be summarized as counts and percentages. For further details, please see section 14. 0 statistical methods of full protocol version 2.0 attached.

The planned primary analysis will be the proportion of patients who following treatment have achieved a SVR at 12 weeks following completion of treatment.

Secondary analyses will determine (a) proportion of patients for whom third party approval for Zepatier treatment was successfully obtained (b) logistic barriers to getting third party approval (c) adverse events with treatment

The design of this protocol does not require any specific statistical methods to test the hypothesis

Power/Sample Size:

A sample size to determine adequate statistical power is not applicable to this protocol since there is only one treatment group and the outcome is binary (SVR at 12 weeks achieved or not achieved) . However, the sample size of approximately 30 patients chosen for this study will be adequate to test the hypothesis and meet the objectives of this study

There are no documents attached for this item.

Data confidentiality

Paper-based records will be kept in a secure location and only be accessible to personnel involved in the study.
Computer-based files will only be made available to personnel involved in the study through the use of access privileges and passwords.
Prior to access to any study-related information, personnel will be required to sign statements agreeing to protect the security and confidentiality of identifiable information.
Wherever feasible, identifiers will be removed from study-related information.

Subject Confidentiality

- Methods to shield participants' identity adequately protect participant privacy.

The long-range plan for protecting the confidentiality of research data, including a schedule for destruction of identifiers associated with the data.

Study information will be kept confidential in accordance with institutional policies and HIPAA.The investigator will retain study medication disposition records, copies of CRFs (or electronic files), and source documents for the maximum period required by the country in which the study will be conducted, or the period specified by the Sponsor, whichever is longer. If the investigator withdraws from the study (e.g., relocation, retirement), the records should be transferred to a mutually agreed upon designee (e.g., another investigator, IRB). Notice of such transfer will be provided in writing to the sponsor.At the end of the study, we plan to destroy the link for the data set to any subject identifiers. No secondary use of the data will be attempted after study end without subsequent IRB approval.

Sensitive Research Information*

Does this research involve collection of sensitive information about the subjects that should be excluded from the electronic medical record? [NOTE: This does not apply to: 1) research information that would not normally be included in the electronic medical record or 2) information that is in the electronic medical record as part of clinical care.]
No

Subject Privacy

Privacy refers to the person's desire to control access of others to themselves. Privacy concerns people, whereas confidentiality concerns data. Describe the strategies to protect privacy giving consideration to the following:

- The degree to which privacy can be expected in the proposed research and the safeguards that will be put into place to respect those boundaries.
- The methods used to identify and contact potential participants.
- The settings in which an individual will be interacting with an investigator.
- The privacy guidelines developed by relevant professions, professional associations and scholarly disciplines (e.g., psychiatry, genetic counseling, oral history, anthropology, psychology).

During their dialysis session, patients will be approached by the study team in person to assess their interest in study participation. Those who are interested in participation will have further discussion regarding the study in a private clinic room in the dialysis unit while they are present for their standard of care visits. All patients to be approached are already part of our dialysis practice and are familiar with the study team. Face to face interactions with the patient will take place in private clinic rooms in our dialysis unit. Discussion of subjects enrolled in this study will be limited to the study team, relevant physicians participating in the care of the subject and the sponsor. When discussing subjects with the sponsor, only de-identified information will be available ie. Each subject will be given a unique study number. All data will be stored in the research office, which is locked for added security. Members of health authorities, the University of Pennsylvania Institutional Review Board or other persons required by law may review the data provided. This data may also be used in publications about the study drug. However, patients identity will not be revealed in any compilations, study reports or publications. Representatives from the sponsor, sponsor affiliates, health authorities and the IRB/IEC may access patients medical records. Such checks will only be done by qualified and authorized personnel. All such persons are required to and will keep the data confidential.

Data Disclosure

Will the data be disclosed to anyone who is not listed under Personnel? If so, identify disclosures.
Members of health authorities, the University of Pennsylvania Institutional Review Board or other persons required by law may review the data provided. This data may also be used in publications about the study drug. However, patients identity will not be revealed in any compilations, study reports or publications. Representatives from the sponsor, sponsor affiliates, health authorities and the IRB/IEC may access patients medical records. Such checks will only be done by qualified and authorized personnel. All such persons are required to and will keep the data confidential.

Protected Health Information/Data Protection*

Name
All elements of dates (except year) for dates directly related to an individual and all ages over 89
Medical record numbers

Does your research request both a waiver of HIPAA authorization for collection of patient information **and** involve providing Protected Health Information ("PHI") that is classified as a "limited data set" (city/town/state/zip code, dates except year, ages less than 90 or aggregate report for over 90) to a recipient outside of the University of Pennsylvania covered entity?
No

Tissue Specimens Obtained as Part of Research*

Are Tissue Specimens being obtained for research?
No

Tissue Specimens - Collected during regular care*

Will tissue specimens be collected during regulator clinical care (for treatment or diagnosis)?

Tissue Specimens - otherwise discarded*

Would specimens otherwise be discarded?

Tissue Specimens - publicly available*

Will tissue specimens be publicly available?

Tissue Specimens - Collected as part of research protocol*

Will tissue specimens be collected as part of the research protocol?

Tissue Specimens - Banking of blood, tissue etc. for future use*

Does research involve banking of blood, tissue, etc. for future use?

Genetic testing

If genetic testing is involved, describe the nature of the tests, including if the testing is predicative or exploratory in nature. If predictive, please describe plan for disclosing results to subjects and provision of genetic counseling.

- Describe how subject confidentiality will be protected

Note: If no genetic testing is to be obtained, write: "Not applicable."

not applicable

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Basic Info | Personnel | Bio | Sponsors | Sites | Protocol | Populations | Procedures | Consents | Risk/Benefit | Confirmation

Protocol Form - Consent

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1. Consent Process

Overview

A written informed consent form (ICF) that shall be approved by the same institutional review board/ independent ethics committee (IRB/IEC) responsible for approval of this protocol. Each ICF shall include the elements required by the ICH Good Clinical Practice (GCP) Guideline and local regulatory requirements and must adhere to the ethical principles that have their origin in the Declaration of Helsinki. The investigator agrees to obtain approval from the sponsor of any written ICF used in the trial, prior to submission to the IRB/IEC. Written informed consent will be obtained from all subjects. Investigators may discuss the availability of the trial and the possibility for entry with a potential subject without first obtaining patient consent. As part of this process, the investigator or qualified investigator designee (who have taken care of the patient as part of their routine post-transplant care) may contact potentially eligible patients via telephone (ahead of their scheduled clinic visit) to ask if they would like to have a sample informed consent emailed or mailed to them ahead of their scheduled outpatient transplant visit to review, in anticipation of discussing it further at their scheduled clinic visit. A phone script is attached to this application for review as well as a cover letter to go with a sample copy of the informed consent if the patient expresses interest in reviewing. The patient will not be contacted without permission from the eligible recipient's transplant nephrology clinic provider first, who are also the investigators on this protocol. Patients will be instructed that their willingness to participate will not affect their eligibility for any medical services at HUP, at any time. Thereafter, once the appropriate essential information has been provided to the subject face to face and fully explained in laymans language by the investigator (or a qualified designee) and it is felt that the subject understands the implications of participating, the IRB/IECapproved written ICF shall be personally signed and dated by both the subject and the person obtaining consent (investigator or designee), and by any other parties required by the IRB/IEC. The study coordinator will be available to answer any questions the patient might have as well. Informed consent will take place in the outpatient renal clinic located at PCAM, The subject shall be given a copy of the signed ICF; the original shall be kept on file by the investigator. All of the above mentioned activities must be completed prior to the subjects participating in the trial.Study subjects will be kept apprised of information specific to the study to ensure an ongoing informed consent will continue throughout the study. If the researchers develop or learn of significant new findings during the study that may affect a subjects willingness to continue to participate, they will contact them. If new information is provided to subjects after having joined the study, they may be asked to sign a new consent document to continue participation. However, informed consent must be obtained and documented prior to initiation of any procedures that are performed solely for the purpose of determining eligibility for this trial.

Children and Adolescents

No children or adolescents will be enrolled in this trial as we are an adult dialysis unit

Adult Subjects Not Competent to Give Consent

- What is the likely degree of impairment? How will competency be assessed (eg, informal assessment by the investigator, mini-mental status exam, formal psychiatric evaluation)?
  Note: *The methods of assessment of competence should be based on the population to be studied and the likelihood of cognitive or decisional impairment in that population.*
- Will consent be obtained from a legally authorized representative, from whom will consent be obtained? Refer to the IRB Policy 705, Surrogate Consent/Authorization for guidance.
- Will subject assent be obtained? If no, provide justification.
  Note: *Respect for persons requires that assent (or at least lack of active dissent) be obtained in most cases.*

We will be inlcuding only competent adults to participate due to the intensity of this trial

2. Waiver of Consent

Waiver or Alteration of Informed Consent*

No Waiver Requested

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Protocol Form - Risk / Benefit

Potential Study Risks

Zepatier is FDA approved to treat Hepatitis C in dialysis patients. Therefore the risks of participating in this study are the same as the subject would encounter being treated with Zepatier in a non-study setting. These risks include side effects of nausea, headache and fatigue. There is the possibility of Hepatitis B reactivation with any treatment for Hepatitis C in patients who are co-infected, therefore we will monitor Hepatitis B levels in patients who are co-infected and if detectable, institute treatment for Hepatitis B in consultation with hepatology. When treating Hepatitis C there is always the possibility of liver inflammation and increases in LFTs, we will monitor these every 4 weeks. Patients with advanced liver disease (ie cirrhosis) are at risk for hepatic decompensation when being treated for Hepatitis C - we will not treat patients with cirrhosis ourselves, but instead refer them to hepatology and let hepatology manage their treatment.Patients who are on warfarin may have a Zepatier-Warfarin drug interaction - in these patients Protime and INR will be monitored weekly during the study

Potential Study Benefits

This study will provide clear benefit to participants as they will be treated for their Hepatitis C infection at no cost to them. They will also add to the general medical knowledge by demonstrating the feasibility of general nephrologists treating Hepatitis C infection and identifying the difficulties in achieving this.

Alternatives to Participation (optional)

If the participant chooses not to participate in this study, their doctor will continue to follow the standard of care practices at the University of Pennsylvania Health-System. The participant can also discuss this with their doctor at any time

Data and Safety Monitoring

- **Note:** Clinical trials (studies involving assessment of medical interventions) must have a monitoring plan appropriate for the potential risks and the complexity of the trial. Monitoring plans describe how a monitor, independent of the study team, regularly inspects study records to ensure the study is adhering to the study protocol and applicable research regulations and Penn requirements. Rather than describe the full detailed monitoring plan here, summarize the key attributes of that plan, and attach the more detailed plan to the main study protocol. Monitoring plans do not necessarily require the use of an independent Data and Safety Monitoring Board (DSMB). Such independent boards are usually reserved for high-risk phase I studies, or large, multi-center phase III trials. Federally funded studies may require the use of an independent DSMB. For more information on monitoring plans, see the Penn Manual for Clinical Research and the section on such plans: **www.med.upenn.edu/pennmanual/sp/mpd/index.html.**
- You may upload additional documentation using the **Upload** button below

Please indicate who will monitor this study in the text box below. Common examples may include:

- Principal Investigator

- Sponsor or contract research organization
- NCI sponsored cooperative group
- Cancer Center (if mandated by CTSMRC)
- Medical monitor
- Safety monitoring committee
- Data and safety monitoring board

The Principal Investigator and Sponsor or contracting research organization will monitor the trial.

There are no documents attached for this item.

Risk / Benefit Assessment

- Assess the ratio of the benefit to be obtained from the study relative to the risks involved. The risks of participation in the research must be balanced by the potential benefits of the research to potential subjects and/or society.
- **Note**: "Minimal risk" means that the risks of harm anticipated in the proposed research are not greater, considering probability and magnitude, than those ordinarily encountered in daily life or during the performance of routine physical and psychological examinations or tests.

The risks of participating in the study are similar to the risks the subject would encounter being treated for Hepatitis C outside of the study setting and the benefit to be obtained is significant as study subjects will have access to Hepatitis C treatment free of charge. Given that all laboratory testing to be performed will be done as per standard of care and obtained from the patients while they are already on dialysis, this is a minimal risk study.

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Basic Info	Personnel	Bio	Sponsors	Sites	Protocol	Populations	Procedures	Consent	Risk/Benefit	Confirmation

Protocol Form - Status

Documents already attached on previous pages

Procedures (studyprocedures.docx) Date uploaded: 02/27/2018 10:27:30 AM

Additional forms or documents

Cover Letter (with additional information that may help in the review)

The following documents are currently attached to this item:

Cover Letter (irbhepccoverletterresponse.docx) Date uploaded: 07/15/2018 06:36:12 AM
Cover Letter (merckcoverletter.docx) Date uploaded: 02/27/2018 10:53:56 AM

Full sponsor's protocol

The following documents are currently attached to this item:

Full sponsor's protocol (irb-studyprotocoltrackedchangeszepatierinhepatitiscinhemodialysis7-14-18.doc) Date uploaded: 07/15/2018 06:37:05 AM
Full sponsor's protocol (irb-studyprotocolcleanversion-zepatierinhepatitiscinhemodialysis7-14-18.doc) Date uploaded: 07/15/2018 06:37:39 AM
Full sponsor's protocol (merckmispprotocoltemplate11-14-17version2.doc) Date uploaded: 02/27/2018 10:47:35 AM

Grant Application (minus the appendices & budget information, for federally-funded studies, e.g. NIH, CDC, DOD)
There are no documents attached for this item.

Performance site approvals for sites other than Penn (this does not apply to other participating sites which have their own IRB.)
There are no documents attached for this item.

Informed consent form (and parental permission/assent form for research involving children)

The following documents are currently attached to this item:

Informed consent form (irb-informedconsentformtrackedchangeszepatierinhepatitiscinhemodialysis7-14-18.doc) Date uploaded: 07/15/2018 06:39:11 AM
Informed consent form (irb-informedconsentform-cleandraft-zepatierinhepatitiscinhemodialysis7-14-18.doc) Date uploaded: 07/15/2018 06:38:25 AM
Informed consent form (pennirbinformedconsentformmerckfinal2-20ds.doc) Date uploaded: 02/27/2018 10:49:55 AM

HIPAA Authorization or Waiver (if applicable)

There are no documents attached for this item.

Investigator's brochure/product labeling (for research involving investigational drugs or devices)

There are no documents attached for this item.

Supporting documents

Supplemental form(s) for research involving pregnant women, fetuses, neonates, prisoners, or children

There are no documents attached for this item.

Questionnaires, inventories surveys, diaries, personality tests, quality of life assessment or other surveys or inventories, data collection forms to be completed by subjects, interview & focus group scripts, consent and recruitment scripts.

There are no documents attached for this item.

All recruitment materials, including advertisements, brochures, letters to patients, transcripts of all broadcast materials, etc, if available. Otherwise submit when available for expedited review.

There are no documents attached for this item.

If you have additional forms or documents to attach to this protocol, please upload them here

There are no documents attached for this item.

This Protocol is currently Assigned to IRB #1.

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